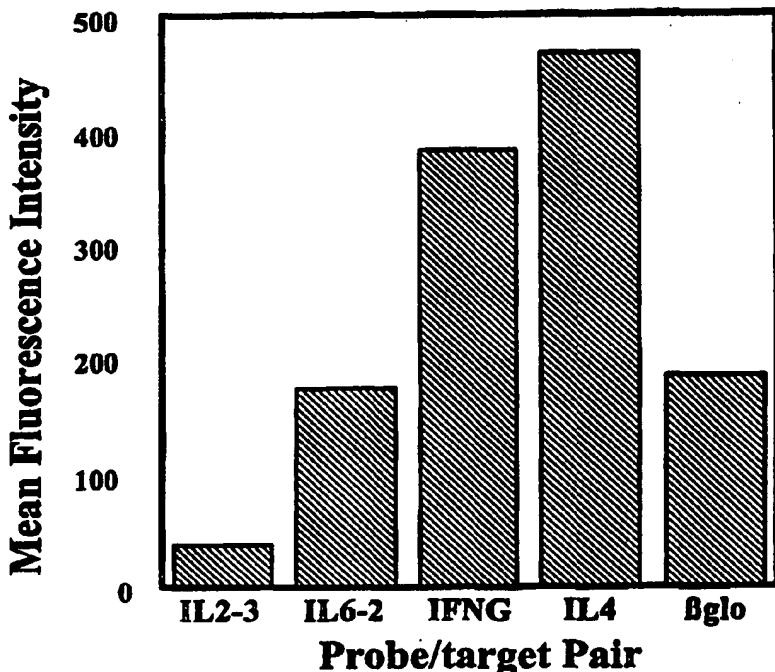




## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<p>(21) International Application Number: <b>PCT/US98/09163</b></p> <p>(22) International Filing Date: 5 May 1998 (05.05.98)</p> <p>(30) Priority Data: 08/851,203 5 May 1997 (05.05.97) US</p> <p>(71) Applicant (for all designated States except US): TRUSTEES OF TUFTS COLLEGE [US/US]; Tufts University, Ballou Hall, Medford, MA 02155 (US).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only): WALT, David, R. [US/US]; 4 Candlewick Close, Lexington, MA 02178 (US). HEALEY, Brian, G. [US/US]; 577 Nortontown Road, Guilford, CT 06437 (US). FERGUSON, Jane, F. [US/US]; Apartment 3, 111 Woodstock Street, Somerville, MA 02144 (US).</p> <p>(74) Agent: CREEHAN, R., Dennis; P.O. Box 750070, Arlington Heights, MA 02175-0070 (US).</p>		<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>Published With international search report.</p> <p>(88) Date of publication of the international search report: 4 February 1999 (04.02.99)</p>	
<p>(54) Title: FIBER OPTIC BIOSENSOR FOR SELECTIVELY DETECTING OLIGONUCLEOTIDE SPECIES IN A MIXED FLUID SAMPLE</p> <p>(57) Abstract</p> <p>The present invention provides biosensors, apparatus and methods for selectively detecting at least one complementary oligonucleotide target specie in a fluid sample containing a mixture of different oligonucleotide fragments. One preferred embodiment of the biosensor is as a unitary fiber optic array having an in-situ hybridization zone comprising not less than one species of single stranded oligonucleotide disposed as individual deposits in aligned organization upon multiple strand end faces at differing spatial positions on the distal array end surface. In this manner, a collective of deployed, single specie, multiple fixed probes are presented for selective in-situ hybridization on-demand with at least one mobile complementary target specie ultimately bearing a joined identifying label. The biosensor provides for optical detection of in-situ hybridization on the distal end surface via the presence of the concomitantly disposed joined identifying label at the differing spatial positions.</p>			



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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/09163

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 G01N21/77 G01N21/64 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 723 146 A (SRI INTERNATIONAL) 24 July 1996 see page 31, line 9 - line 32 see figure 23 ---	1, 4
Y	US 5 244 636 A (WALT) 14 September 1993 cited in the application see abstract see column 4, line 53 - column 5, line 9 see column 5, line 58 - column 7, line 9 see column 8, line 40 - line 43 see column 24, line 34 - line 56 see column 26, line 3 - line 35 see figures 17, 18 ---	2, 3, 5-8
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Date of the actual completion of the international search	Date of mailing of the international search report
28 October 1998	05/11/1998
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Thomas, R.M.

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International Application No

PCT/US 98/09163

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 478 319 A (TOSHIBA) 1 April 1992 see page 4, line 1 - line 15 see page 6, line 47 - page 7, line 6 see examples 2,6,9,12,13 ----	1,4
X	US 5 002 867 A (MACEVICZ) 26 March 1991 see abstract see column 8, line 4 - line 27 ----	1,4
X	EP 0 269 764 A (MOLECULAR BIOSYSTEMS) 8 June 1988 see page 2, line 4 - line 5 see page 6, line 38 - line 40 -----	1,4

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/US 98/09163

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
EP 0723146	A 24-07-1996	AT 170004	T	15-09-1998	
		CA 2144527	A	31-03-1994	
		DE 69320484	D	24-09-1998	
		EP 0660936	A	05-07-1995	
		JP 8501632	T	20-02-1996	
		WO 9407142	A	31-03-1994	
		US 5674698	A	07-10-1997	
		US 5736410	A	07-04-1998	
US 5244636	A 14-09-1993	US 5244813	A	14-09-1993	
		US 5320814	A	14-06-1994	
		US 5250264	A	05-10-1993	
EP 0478319	A 01-04-1992	DE 69125441	D	07-05-1997	
		DE 69125441	T	06-11-1997	
		JP 2573443	B	22-01-1997	
		JP 5199898	A	10-08-1993	
		US 5776672	A	07-07-1998	
US 5002867	A 26-03-1991	EP 0439550	A	07-08-1991	
		JP 4501362	T	12-03-1992	
		WO 9004652	A	03-05-1990	
EP 0269764	A 08-06-1988	GR 3003056	T	17-02-1993	